Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-124 are pending in this application and are rejected on various grounds. Claim 124 has been canceled without prejudice or disclaimer. Solely in the interest of expediting prosecution in this case, Applicants have amended Claim 119 to remove references to Figures and to recite "an antibody or fragment thereof" that bind to the polypeptide SEQ ID NO: 314. The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the 'Mixed lymphocyte reaction' assay for patentable utility in this case. This utility was first disclosed in International Application PCT/US00/05841, filed March 2, 2000, priority for which has been claimed in this application. Further, the PRO1346 sequence and the nucleic acid encoding it was first disclosed in U.S. Provisional application 60/097661, filed 8/24/1998, (as SEQ ID NO: 2 and 1), priority for which has also been claimed in this application. Hence, the present application is at least entitled to an effective filing date of **March 2, 2000.**

Information Disclosure Statement

Applicants submit an IDS separately enlisting references recited in the Blast report in order to be compliant with 37 C.F.R. § 1.98(a)(1). Consideration of this Information Disclosure Statement is respectfully requested.

Specification

A. The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

B. Applicants have amended the title to better describe the claimed invention.

Accordingly, Applicants believe that the objections to the specification should be withdrawn.

Claim objections

A. Applicants have amended claims 119 to remove references to Figures in the claim language. Claim 124 has been canceled and hence this rejection should be withdrawn.

Claim Rejections – 35 USC § 101 and 35 USC § 112, first paragraph

Claims 119-124 are rejected under 35 U.S.C. §101 allegedly because "the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility". The Examiner asserts that the instant application does not disclose a specific and substantial biological role of this protein or its significance. Claims 119-124 are further rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention". Applicants respectfully disagree with and traverse the rejection.

As discussed above, Applicants submit that they rely on the 'Mixed lymphocyte reaction' assay for patentable utility for PRO1346, and is therefore at least entitled to an effective filing date of **March 2, 2000.**

Utility Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used

in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."**

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.**

Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Further, the legal standard with respect to *in vitro* or animal model data providing pharmacological activity has been commented on in *Cross v. Iizuka*, 753 F.2nd 1040, 1051, 224 USPQ 739, 747-48 (Fed. Cir. 1985):

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing

an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vitro* utility."

Furthermore, M.P.E.P. 2107.03 (III) states that:

"If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition or process."

Thus, the legal standard accepts that *in vitro* or animal model data is acceptable utility as long as the data is "reasonably correlated" to the pharmacological utility described.

Arguments

PRO1346 has utility

Without acquiescing to the propriety of this rejection, but solely in the interest of expediting prosecution in this case, Applicants submit a declaration with supportive references from the art to show that PRO1346 has immunostimulant activity and therefore, antibodies to PRO1346 have utility as immunosuppressors.

Applicants submit a declaration by Sherman Fong, Ph.D. of Genentech, Inc., an expert in the field of Immunology and co-inventor of the present application, to show that there are specific immune stimulant utilities for compounds identified by an MLR assay. The Declaration explains how the MLR reaction was performed in the instant application using peripheral blood mononuclear cells (PBMCs), which contain responder T-cells, and allogenic, pre-treated (irradiated) PBMCs, which predominantly contained dendritic cells. As Dr. Fong emphasizes, immunostimulants are important and are very desirable in the treatment of cancer and in enhancing the effectiveness of previously identified treatments for cancer. Supportive evidence also comes from teachings in the art like Steinman *et al.* (Exhibit B) who states that "...**medicine needs therapies that enhance immunity or resistance to infections and tumors**. (page 1, column 1, line 7; emphasis added)". Further teachings like Peterson *et al.* (Exhibit D) show that, recently, the immune stimulant IL-12, was successfully used in a cancer vaccine trial to treat melanoma. Further, as Dr. Fong explains regarding the IL-12 melanoma trial:

"Due to the immune stimulatory effect of IL-12, **the treatment provided superior results** in comparison to earlier work, where the patients' own dendritic cells were prepared from peripheral blood mononuclear cells (PBMCs) treated with antigens, then cultured *in vitro* and returned to the patient to stimulate anti-cancer response" (Emphasis added).

Further, Dr. Fong's declaration clearly states that:

"A PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity exhibited by IL-12 and would find practical utility as an immune stimulant".

Accordingly, the positive results obtained in this assay clearly establish the stated utility for the polypeptides claimed and accordingly, the nucleic acids encoding these polypeptides also have utility. The specification, in turn, enables one skilled in the art to use the compounds for the asserted purpose.

By the foregoing arguments and supportive evidence, Applicants have established that the MLR reaction is a generally recognized assay to assess immunostimulatory activity and is useful in the treatment of viral infections like HIV or Epstein Barr viral infections or cancers like melanoma. Antibodies to PRO1346 are useful as immunosuppressors which are useful, for example, to treat during graft rejection. Further, since the legal standard accepts *in vitro* as acceptable utility and the data is "reasonably correlated" to the pharmacological utility based on the discussions above, a valid case for utility has been made and would be considered credible by a person of ordinary skill in the art.

In view of the foregoing arguments and submitted evidence, the Examiner is respectfully requested to reconsider and withdraw the present rejections.

Claim Rejections – 35 USC § 112, second paragraph

A. Claims 122 was rejected under 35 U.S.C. §112, second paragraph for being indefinite. The Examiner alleges that it was unclear how an antibody can be both an antibody and a fragment.

Applicants have amended claim 122 to recite "an antibody, or a fragment thereof" and therefore this rejection should be withdrawn.

B. Claim 124 was rejected for lack of clarity in reciting "specifically binds" since, allegedly, this term was not defined in the specification. Without acquiescing to the propriety of this rejection and solely in the interest of expedited prosecution in this case, Applicants have canceled claim 124 and therefore, this rejection is moot. Further, Applicants submit that the art-recognized meaning of "specifically binds" is that the antibody binds to a particular antigen and does not significantly cross-react with another antigen. Accordingly, this rejection should be withdrawn.

Claim Rejections – 35 USC § 102

A. Claims 119-124 are rejected under 35 U.S.C. §102(b) as being anticipated by Baker (WO99/63088- dated December 1999).

As discussed under the section of priority, the PRO1346 sequence and its encoding nucleic acid was first disclosed in U.S. Provisional application 60/097661, **filed 8/24/1998**, (as SEQ ID NO: 2 and 1), priority for which has been claimed in the instant application. Further, the cited Baker publication is the PCT/US99/12252 application, to which priority has also been claimed in the instant application. Therefore, Baker *et al.* is not prior art and Applicants request that this rejection be withdrawn.

B. Claims 119-124 are rejected under 35 U.S.C. §102(b) as being anticipated by Fernandez (WO00/61754- dated October 2000).

As discussed above, based on the effective priority date of **March 2, 2000** entitled to this application, Fernandez is not prior art. Thus, this rejection is moot and should be withdrawn.

C. Claims 119-124 are rejected under 35 U.S.C. §102(b) as being anticipated by Zhao (Hum. Mol. Genetics - dated 1995).

Amended claim 119 recites an antibody that binds "specifically" to the polypeptide of PRO1346. Applicants submit that the art-recognized meaning of "specifically binds" is that the antibody binds to a particular antigen and does not significantly cross-react with another antigen. In this case, the antibody by Zhao, which has only identical to 8 contiguous amino acids of SEQ ID NO: 314 is not encompassed by claim 119. Accordingly, this rejection should be withdrawn.

Claim Rejections – 35 USC § 103

A. Claims 119-124 are rejected under 35 U.S.C. §103(a) as being unpatentable over Zhao (1990) in view of Fernandez (2000).

As discussed above, Zhao's antibody does not read on amended claim 119 since it does not specifically bind to the polypeptide of SEQ ID NO: 314. Based on the effective priority date entitled to this application, Fernandez falls as prior art. Therefore, present claims are not obvious over Zhao in view of Fernandez and hence, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C24). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 9, 2004

Daphne Reddy

Daphne Reddy
Reg. No. 53,507

HELLER EHRMAN WHITE & McAULIFFE LLP
Customer No. 35489
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638
2016618